

## CARDIOVASCULAR MEDICINE

# Hypertension control at hospital discharge after acute coronary event: influence on cardiovascular prognosis—the PREVENIR study

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**Objective:** To assess hypertension control in patients admitted to hospital for an acute coronary event and to investigate the influence on prognosis of controlling hypertension before hospital discharge.

**Design:** Multicentre retrospective cohort study.

**Methods:** The medical records were examined of all patients admitted in 77 cardiological centres on January 1998 for myocardial infarction or unstable angina and who survived. Clinical characteristics, blood pressure at hospital discharge, and cardiovascular events during a six month follow up were recorded.

**Main outcome measures:** Cardiovascular deaths and non-fatal myocardial infarction.

**Results:** Data were available in 1247 patients. At discharge, 411 (32.9%) had uncontrolled hypertension; among these, 276 (22.1%) were uncontrolled on the basis of systolic blood pressure alone. Forty three cardiovascular deaths and 20 non-fatal myocardial infarcts occurred during follow up. In a multivariate analysis, age, left ventricular ejection fraction, previous history of cardiovascular disease, and isolated systolic hypertension (odds ratio 1.9, 95% confidence interval 1.07 to 3.37) were associated with the outcome.

**Conclusions:** 22.1% of patients admitted to hospital for an acute coronary syndrome have uncontrolled isolated systolic hypertension on discharge. This appears to be an independent predictor of cardiovascular outcome.

Patients with coronary heart disease are a priority for preventive cardiology. The EUROASPIRE (European action on secondary prevention through intervention to reduce events) surveys<sup>1,2</sup> conducted in nine countries in 1995–1996 and 1999–2000 underlined the lack of any improvement in blood pressure management during this period in patients with established coronary heart disease. Six months after a hospital admission for an acute coronary event or coronary revascularisation, the proportion of patients with high blood pressure ( $\geq 140/90$  mm Hg) was virtually the same in the two surveys (55.4% v 53.9%). Whether hypertension fails to be controlled during the hospital stay or whether hypertension control worsens after hospital discharge is not known. There are, indeed, few data about hypertension control during hospital admissions, and little is known about the influence of blood pressure control early after an acute coronary event on cardiovascular prognosis.<sup>3</sup>

Our aims in this study were to assess hypertension control in a large sample of patients admitted to hospital for an acute coronary event and to investigate the effect of controlling hypertension before hospital discharge.

## METHODS

### Study design

A cohort study was conducted in France in 77 cardiological centres, including public and private hospitals, among which 28 were teaching hospitals. The medical records of all patients admitted to the coronary care units of these hospitals on January 1998 were studied retrospectively in June 1998. Patients were eligible for inclusion in the study if they had acute myocardial infarction or unstable angina and survived to discharge from hospital.

Acute myocardial infarction was defined as the presence of at least two of the following three criteria: typical chest pain

lasting for more than 30 minutes; ST segment elevation of more than 0.1 mV in two or more contiguous leads on the initial ECG; serum creatine kinase concentration of more than twice the upper limit of the normal range. Unstable angina was defined as angina at rest, new symptoms of angina, or symptoms of angina that had increased in severity, requiring admission to an intensive care unit. Demographic characteristics, medical history including risk factors, the type of acute coronary syndrome, reperfusion therapy, and left ventricular ejection fraction were recorded for each patient. The last blood pressure measured before discharge from hospital was used in the analysis.

All events occurring between hospital discharge and June 1998 were recorded. Follow up data were obtained from the hospital records in 24.9% of patients. For the remaining subjects, the investigators were instructed to interview first the cardiologist and then the general practitioner.

### Primary outcome

The outcome events studied were cardiovascular deaths and non-fatal myocardial infarction. Cardiovascular deaths included deaths from ischaemic heart disease, stroke, aortoiliac disease, congestive heart failure, and sudden deaths—defined as witnessed deaths that occurred within one hour of the onset of acute symptoms, with no evidence that violence or accident played any role in the fatal outcome.

**Abbreviations:** ASPIRE, action on secondary prevention through intervention to reduce events; EUROASPIRE, European action on secondary prevention through intervention to reduce events; SHEP, systolic hypertension in the elderly program

**Table 1** Baseline characteristics of the study population

	Population (n=1247)
Men	892 (71.5)
Age	
<65 years	544 (43.6)
65–74 years	385 (30.9)
≥75 years	318 (25.5)
BMI (kg/m <sup>2</sup> )	
BMI <25 kg/m <sup>2</sup>	430 (34.5)
25 kg/m <sup>2</sup> ≤ BMI <30 kg/m <sup>2</sup>	396 (31.8)
BMI ≥30 kg/m <sup>2</sup>	136 (10.9)
Unavailable	285 (22.8)
Unstable angina	557 (44.7)
Myocardial infarction	690 (55.3)
Anterior location of MI*	265 (38.9)
Thrombolysis*	190 (27.5)
LVEF <40%†	129 (10.3)
Previous history	
Myocardial infarction	278 (22.3)
Peripheral artery disease	125 (10.0)
Stroke	65 (5.2)
Cardiovascular risk factors before hospital admission‡	
Smoking	490 (39.3)
Dyslipidaemia	579 (46.4)
Hypertension	596 (47.8)
Diabetes	261 (20.9)
Treatment on discharge	
β Blockers	857 (68.7)
ACE inhibitors	523 (41.9)
Calcium channel blockers	352 (28.2)
Antiplatelet drugs	1159 (92.9)
Statins	449 (36.0)

\*Among patients with myocardial infarction.

†In 70 patients, left ventricular ejection fraction was not available; the percentage was calculated on the remaining 1177 patients.

‡Cardiovascular risk factors before hospital admission defined as a documented history of hypertension, dyslipidaemia, diabetes or smoking habits reported in medical records.

ACE, angiotensin converting enzyme; BMI, body mass index; LVEF, left ventricular ejection fraction; MI, myocardial infarction.

## Analysis

Patients lost to follow up or who died from unknown or non-cardiovascular causes were excluded from the analysis.

Patients were categorised according to their hypertension status: normotensive, controlled hypertensive, and uncon-

trolled hypertensive. *Normotension* was defined as a blood pressure of < 140/90 mm Hg without a history of arterial hypertension. *Controlled hypertension* was defined as a history of hypertension and a blood pressure of < 140/90 mm Hg. *Uncontrolled hypertension* was defined as blood pressure ≥ 140/90 mm Hg. Among the uncontrolled hypertensive subjects we distinguished patients with *isolated systolic hypertension* (a diastolic blood pressure of < 90 mm Hg and a systolic blood pressure of ≥ 140 mm Hg), *systolo-diastolic hypertension* (a diastolic blood pressure of ≥ 90 mm Hg and a systolic blood pressure of ≥ 140 mm Hg), and *isolated diastolic hypertension* (a systolic blood pressure of < 140 mm Hg and a diastolic blood pressure of ≥ 90 mm Hg).

The groups were compared using  $\chi^2$  tests. The relations between cardiovascular outcome, hypertension status, cardiovascular risk factors, and clinical characteristics were assessed using a backward logistic regression. In view of the aims of the study—and as hypertension status, systolic blood pressure, and diastolic blood pressure were closely correlated—we chose to use only hypertension status in the model. All variables that were significant ( $p < 0.05$ ) in bivariate analysis were entered into the model. Statistical analysis was performed on SAS statistical software (SAS/STAT user's guide, release 6.12. Cary, North Carolina, USA: SAS Institute Inc, 1997).

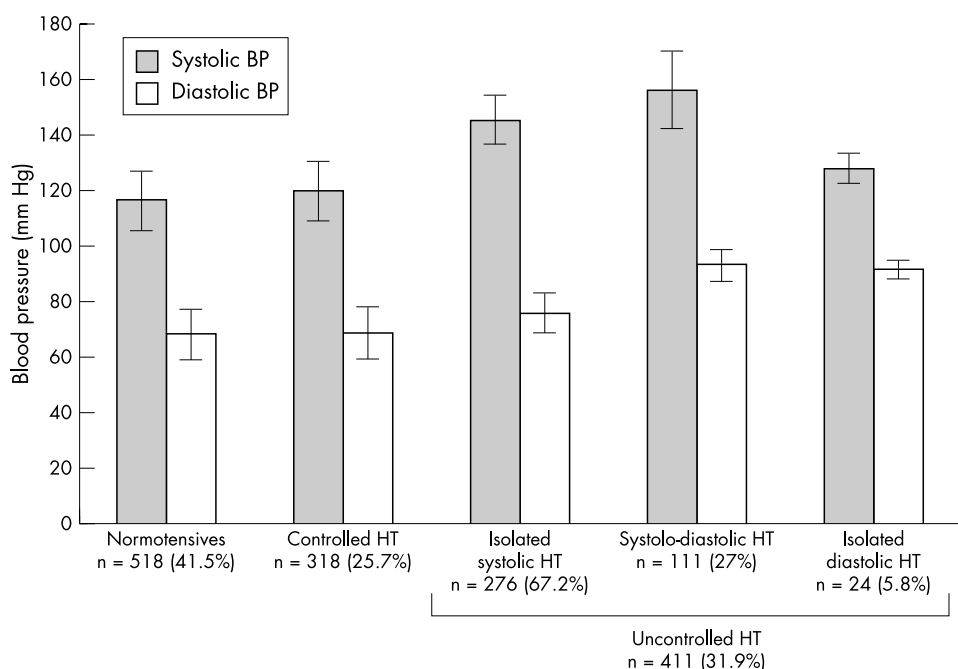
## RESULTS

### Study population

In all, 1394 patients were eligible for the study. In 1327 of these, blood pressure was measured at hospital discharge and information about previous history and risk factors for cardiovascular disease was available. Of these 1327 patients, 58 were lost to follow up and 22 died from unknown causes ( $n = 9$ ) or from non-cardiovascular causes ( $n = 13$ : eight from carcinoma, three from sepsis, one from acute renal failure, and one from haemoptysis) and were excluded from the analysis. Thus 1247 patients formed the basis of this report. The baseline characteristics of the study population are presented in table 1.

### Blood pressure status

The blood pressure profile of the study population is shown in fig 1. At hospital discharge, 518 patients (41.5%) were normotensive, 318 (25.5%) had controlled hypertension, and 411 (32.9%) had uncontrolled hypertension, of whom 276 (22.1%) were uncontrolled on the basis of systolic blood pressure



**Figure 1** Blood pressure profile in the study population. BP, blood pressure; HT, hypertensive subjects.

**Table 2** Demographics and clinical characteristics: bivariate analysis with primary outcome as dependent variable

Variable	Primary outcomes (n (%))	p Value	Odds ratio	95% CI
Age (years)		0.001		
<65 (n=544)	13 (2.4)	–	1	–
65–75 (n=385)	12 (3.1)	0.50	1.31	0.59 to 2.91
≥75 (n=318)	38 (12)	0.001	5.54	2.90 to 10.58
Sex				
Men (n=892)	36 (4.0)	–	1	–
Women (n=355)	27 (7.6)	0.009	1.96	1.17 to 3.28
Diagnosis at entry				
Unstable angina (n=557)	19 (3.4)	–	1	–
Myocardial infarction (n=690)	44 (6.4)	0.01	1.93	1.11 to 3.34
Left ventricular ejection fraction		0.001		
>40% (n=983)	40 (4.0)	–	1	–
≤40% (n=129)	15 (11.6)	0.0004	3.1	1.66 to 5.79
Unavailable (n=135)	8 (5.9)	0.32	1.48	0.68 to 3.24
Previous history of myocardial infarction				
No (n=969)	40 (4.1)	–	1	–
Yes (n=278)	23 (8.3)	0.005	2.09	1.23 to 3.56
Previous history of peripheral artery disease				
No (n=1122)	50 (4.5)	–	1	–
Yes (n=125)	13 (10.4)	0.004	2.49	1.31 to 4.72
Previous history of stroke				
No (n=1182)	56 (4.7)	–	1	–
Yes (n=68)	7 (10.8)	0.04	2.43	1.06 to 5.56
Cardiovascular risk factors before hospital admission*				
Smoking				
No (n=757)	47 (6.2)	–	1	–
Yes (n=490)	16 (3.3)	0.02	0.51	0.29 to 0.91
Dyslipidaemia				
No (n=668)	42 (6.3)	–	1	–
Yes (n=579)	21 (3.6)	0.03	0.56	0.33 to 0.96
Diabetes				
No (n=986)	40 (4.0)	–	1	–
Yes (n=261)	23 (8.8)	0.001	2.29	1.34 to 3.89

\*Cardiovascular risk factors before hospital admission defined as a documented history of hypertension, dyslipidaemia, diabetes, or smoking habits reported in medical records.  
CI, confidence interval.

alone. In the population as a whole, systolic blood pressure was slightly higher in controlled hypertensive subjects than in normotensive subjects, while diastolic blood pressure was similar. As expected, both systolic and diastolic blood pressure were significantly higher in subjects with uncontrolled hypertension than in those with controlled hypertension or in normotensive subjects.

#### Blood pressure status and cardiovascular prognosis

The primary outcome occurred in 63 patients during the follow up period: 43 cardiovascular deaths and 20 non-fatal myocardial infarcts. In bivariate analysis (table 2), cardiovascular outcome was significantly associated with age, sex, diagnosis at entry, previous history of myocardial infarction, stroke and peripheral arterial disease, diabetes, the use of  $\beta$  blockers,

the use of statins, left ventricular ejection fraction, and isolated systolic hypertension. A non-significant trend was observed with uncontrolled hypertension, while no significant relation was observed with systolo-diastolic hypertension. In multivariate analysis (tables 3 and 4), age, left ventricular ejection fraction, isolated systolic hypertension, and a previous history of myocardial infarction or peripheral arterial disease were significantly associated with the outcome.

## DISCUSSION

### Representativeness of the data

The 1998 survey involved a large sample of patients recruited from 77 cardiological centres: 28 university hospitals, 41 general hospitals, and eight private clinics (specialising in cardiology),

**Table 3** Hypertension status: bivariate analysis with primary outcome as dependent variable

Hypertension status at discharge	Primary outcomes (n (%))	p Value	Odds ratio	95% CI
<i>Hypertension status</i>		0.13		
Normotensive (n=518)	21 (4.1)	–	1	–
Controlled HT (n=318)	14 (5.8)	0.80	1.09	0.55 to 2.17
Uncontrolled HT (n=411)	28 (6.8)	0.06	1.73	0.97 to 3.09
<i>Isolated systolic hypertension</i>				
No (n=971)	41 (4.2)	–	1	–
Yes (n=276)	22 (8.0)	0.01	1.96	1.15 to 3.36
<i>Systolo-diastolic hypertension</i>				
No (n=1136)	58 (5.1)	–	1	–
Yes (n=111)	5 (4.5)	0.78	0.88	0.34 to 2.23

CI: confidence interval; HT, hypertension.

**Table 4** Multivariate analysis with cardiovascular outcome as dependent variable

	Odds ratio ( 95% CI)	p Value
Age		0.0001
<65 years	–	
65 to 75 years	1.29 (0.58 to 2.89)	0.53
≥75 years	4.82 (2.48 to 9.37)	0.0001
Isolated systolic hypertension	1.9 (1.07 to 3.37)	0.02
Left ventricular ejection fraction		0.09
≥40%	–	
<40%	2.1 (1.07 to 4.13)	0.03
Unavailable	1.13 (0.49 to 2.58)	0.77
Diagnosis at entry		0.008
Unstable angina	–	
Myocardial infarction	2.18 (1.22 to 3.92)	
Previous history of peripheral artery disease	2.16 (1.08 to 4.31)	0.02
Previous history of myocardial infarction	1.82 (1.03 to 3.24)	0.04

representing 15.4% (77/501) of all French coronary care units. All categories of hospital were represented, although there was an over-representation of university hospitals and an under-representation of private clinics.

### Hypertension control

The difficulty in controlling hypertension in secondary prevention has been emphasised before. In Canada<sup>4</sup> approximately 20% of patients receiving secondary prevention were found to be hypertensive in primary care. In the ASPIRE study,<sup>5</sup> conducted in the UK, up to one quarter of patients remained hypertensive. In the EUROASPIRE studies,<sup>1,2</sup> six months after a hospital admission for coronary disease about 50% of patients had a raised blood pressure. However, epidemiological data are lacking about blood pressure control at the time of hospital discharge. One of the main findings of our study is that hypertension was uncontrolled at discharge in one third of all patients admitted to hospital for an acute coronary event. Because of prolonged bed rest and enhanced surveillance, predischARGE blood pressure is likely to be an underestimate of follow up blood pressure. These results therefore suggest that an important proportion of hypertensive patients found to be uncontrolled several months after an acute coronary event are uncontrolled during their initial hospital stay. As is the case in primary prevention,<sup>6</sup> we found that arterial hypertension in patients with acute coronary syndromes was uncontrolled mainly on the basis of poor systolic blood pressure control, despite the use of antihypertensive drugs. In this respect, it would be relevant to determine the proportion of patients in this population with “white coat” isolated systolic hypertension—indeed, there are recent data<sup>7</sup> suggesting that most of the benefit of treatment was seen in patients with a daytime systolic blood pressure of  $\geq 160$  mm Hg.

### Cardiovascular prognosis

#### Extent of atheromatous disease

Independently of age and cardiac damage, we showed that after an acute coronary event a previous history of peripheral arterial disease predicts a poor short term cardiovascular prognosis. This is in agreement with previous studies on the long term prognosis of patients with coronary lesions.<sup>8,9</sup> An increased individual susceptibility to atheromatous disease from genetic or environmental factors may account for this relation. On the other hand, diffuse atherosclerotic lesions may have a negative influence on coronary disease through their deleterious effect on arterial compliance.<sup>10–12</sup> Whatever the mechanisms, this finding suggests that after an acute coronary event, patients with previous atheromatous disease require a specific therapeutic strategy.

### Isolated systolic hypertension

We showed that isolated systolic hypertension identified during the hospital stay was an independent predictor of cardiovascular prognosis in patients with acute coronary events, whereas no relation was observed with systolo-diastolic hypertension. Isolated systolic hypertension results in an increase in pulse pressure which may partly account for this result. Indeed the value of pulse pressure in determining prognosis has been established repeatedly,<sup>13–15</sup> as it has in secondary prevention.<sup>16</sup> In randomised trials in which isolated systolic hypertension was the only inclusion criterion, drug treatment resulted in a significant reduction in coronary events, whereas in trials in which the inclusion criterion was primarily diastolic pressure, antihypertensive drugs were not as effective at reducing morbidity and mortality in coronary heart disease as in stroke.<sup>17–20</sup>

### Therapeutic implications

There is evidence that currently available drugs may decrease systolic blood pressure in elderly patients with isolated systolic hypertension.<sup>20,21</sup> A beneficial influence of tight systolic blood pressure control has been suggested: in the SHEP study (systolic hypertension in the elderly program), a reduction in stroke incidence occurred when specific systolic blood pressure goals were attained (a decrease of at least 20 mm Hg from baseline to below 160 mm Hg).<sup>22</sup> However, concerns have been raised about an excessive fall in diastolic blood pressure in atherosclerotic patients, and in a reanalysis of data from the SHEP study,<sup>23</sup> patients with treated hypertension who experienced a cardiovascular event had a lower diastolic blood pressure than those who did not have an event. In the Rotterdam study,<sup>24</sup> which involved elderly hypertensive subjects, the risk of stroke was greater in those given antihypertensive drugs if their diastolic blood pressure was  $< 65$  mm Hg than if it was between 65–74 mm Hg. In the light of these data, it was of interest that in our study subjects with controlled hypertension and normotensive subjects had similar diastolic blood pressures (about 68 mm Hg). Thus our results do not suggest that tight blood pressure control results in an excessive fall in diastolic blood pressure, and better control of isolated systolic hypertension in patients with acute coronary syndromes is likely to improve the cardiovascular outcome in this high risk population.

### Conclusions

Our study shows that an important proportion of patients admitted to hospital for an acute coronary event have uncontrolled hypertension at hospital discharge, mainly because of poor systolic blood pressure control. Isolated systolic hypertension appears to be a powerful and independent predictor of cardiovascular outcome in these patients.



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## IMAGES IN CARDIOLOGY

### Imaging in aortoarteritis

A 20 year old girl had uncontrolled hypertension and absent lower limb pulses. Transoesophageal echocardiography was done. Cross section of the descending aorta at T8 and T9 vertebral level showed an irregular shaped lumen (below left, panel A, arrows; AO, aorta). There was intimal thickening. Long axis imaging showed long segment tight stenosis with the typical rat tail deformity (panel B, arrows) of the lumen. The narrowest diameter was 2 mm while the normal segment above was 11 mm. Non-specific aortoarteritis was

diagnosed. Descending aortic injection confirmed the above findings (below right). There was irregular luminal narrowing with rat tail deformity.

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